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IN THIS ISSUE

Etiology of the Acute Diarrheal Diseases
A Report on the Metabolism of DDT

CONTENTS

	Page
Studies of the acute diarrheal diseases. XII. Etiology. Albert V. Hardy and James Watt	57
The metabolism of 2,2 bis (p-chlorophenyl) 1,1,1 trichloroethane (DDT). I. A metabolite from rabbit urine, di(p-chlorophenyl) acetic acid; its isolation, identification, and synthesis. William C. White and Thomas R. Sweeney	66
Deaths during week ended December 23, 1944	72
PREVALENCE OF DISEASE	
United States:	
Reports from States for week ended December 30, 1944, and comparison with former years	73
Weekly reports from cities:	
City reports for week ended December 23, 1944	77
Rates by geographic divisions, for a group of selected cities	79
Foreign reports:	
Angola—Notifiable diseases—July–September 1944	80
Canada—Provinces—Communicable diseases—Week ended December 9, 1944	80
New Zealand—Notifiable diseases—4 weeks ended December 2, 1944	81
Reports of cholera, plague, smallpox, typhus fever, and yellow fever received during the current week—	
Plague	81
Smallpox	81
Typhus fever	81
* * *	
Court decisions on public health	82

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STUDIES OF THE ACUTE DIARRHEAL DISEASES

XII. ETIOLOGY [1] [2]

By ALBERT V. HARDY, *Surgeon (R)* and JAMES WATT, *Surgeon, United States Public Health Service*

Study of the acute diarrheal diseases was initiated in 1936. Various aspects of the problem were investigated in areas chosen because they were representative of regions of high, very high, medium, and very low reported mortality from dysentery, diarrhea, and enteritis. The areas selected and duration of study are as follows: New Mexico 1936–38, Georgia 1939–40, New York 1939–40 and 1942, and Puerto Rico 1941–42. A representative county in New Mexico and one in Georgia, and a town and a rural community in Puerto Rico were

[1] From the Division of Infectious Diseases, National Institute of Health, with the cooperation of State, Insular, and local health departments of the areas in which the studies were conducted, the Indian Medical Service, and the DeLamar Institute of Public Health, Columbia University.

[2] Other papers in this series are:

Hardy, A. V., Watt, James, DeCapito, T. M., and Kolodny, Maxwell H.: Studies of the acute diarrheal diseases. I. Differential culture media. Pub. Health Rep., 54: 287–300 (Feb. 24, 1939).

Spector, Bertha Kaplan, Hardy, A. V., and Mack, Mary Graham: Studies of the acute diarrheal diseases. II. Parasitological observations. Pub. Health Rep., 54: 1105–1113 (June 29, 1939).

Hardy, A. V., Watt, James, Kolodny, M. H., and DeCapito, T. M.: Studies of the acute diarrheal diseases. III. Infections due to the "Newcastle dysentery bacillus." Am. J. Pub. Health, 30: 53–58 (1940).

Hardy, A. V., Frant, S., Jarcho, S. W., and Schlosser, E. G.: Studies of the acute diarrheal diseases. IV. An outbreak of bacillary dysentery due to the "Newcastle dysentery bacillus." Pub. Health Rep., 55: 2101–2116 (Nov. 15, 1940).

Mosher, W. E., Jr., Wheeler, S. M., Chant, H. L., and Hardy, A. V.: Studies of the acute diarrheal diseases. V. An outbreak due to *Salmonella typhi murium*. Pub. Health Rep., 56: 2415–2426 (Dec. 19, 1941).

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selected for intensive study. The New York data were collected in Manhattan and in selected State institutions.

The following case-finding procedures were used: Physicians in New Mexico and Georgia were requested, through the county medical societies and by personal contacts, to report by telephone all cases of acute diarrhea seen in private practice or in the public health clinics. Pediatricians were particularly interested. In Puerto Rico and in New York City reports were secured from hospitals and health department clinics. Public health nurses in all areas reported cases encountered in their field work. Each case reported from these sources was the focus for an inquiry by our own nurses as to the occurrence of diarrhea in other members of the household or in neighboring families. Each patient was visited by the nurse as soon as practicable to arrange for the collection of fecal specimens; three specimens at daily intervals were requested from current cases, from convalescent, and recently recovered cases, and from all household members when these were being studied. The nurse followed the course of the illness on her return visits for the collection of these specimens.

Most of the detailed epidemiological and clinical histories were obtained by the authors; the remainder by other physicians temporarily assigned to assist in this work (Drs. M. Gutelius in New Mexico, M. Greenberg and E. Schlosser in New York City, and J. S. Peterson in Puerto Rico). A report form was used on which specific items of information were checked or recorded. Repeated visits during illness were not unusual and a final "follow-up" visit was made from two to four months after onset. Each case determined actually to be a diarrheal disease was classified on clinical grounds at the time the history was taken as: Primary diarrhea, diarrhea secondary to some specified condition, "food poisoning," etc., or as "no diarrheal disease." The severity of illness was also noted. These classifications made by one of us were independently reviewed by the other when the data on all cases were tabulated.

In addition to this study of cases and their contacts, representative groups, selected without consideration of the occurrence of diarrheal disease, were studied. Here the prevalence and distribution of *Shigella* infections in the general population were determined by cultural surveys. The methods of obtaining these study groups are stated in the report on cultural surveys of normal population groups.

In each area these data were supplemented by a study of institutional inmates, particularly those among whom *Shigella* infections were prevalent. This revealed the course of the infection in groups of individuals and provided evidence concerning natural immunological responses. Here also the mild disorders clinically unimportant but epidemiologically significant could be observed in their relation to the severe illnesses usually described.

In each area, our own field laboratory was the center of our study. Here we had full-time technical assistants who became highly experienced. Changes in technique were limited to the replacement of a less efficient procedure by a demonstrably superior one. Fecal specimens from the general population were collected in glycerine saline preservative. Ordinarily a sample from a morning movement was obtained, and this was brought to the laboratory and plated in the afternoon. The rectal swab technique was employed on institutional inmates (*1*). After incubation for about 20 hours, suspicious colonies were picked to Russell's double or Krumwiede's triple sugar agar. Those giving a "typhoid-dysentery" reaction were examined by a full series of the usual cultural tests, and by serologic titration with monovalent antiserums as described elsewhere (*2*).

The only major variation in technique was in the differential culture media employed. In 1936 a medium was used which was then regarded as standard, eosin-methylene blue agar. The results with this were so poor when compared with the more highly selective preparations used in subsequent years that the findings for that year are excluded from all tabulated data. One plate of each of four media was employed in 1937, and desoxycholate citrate agar was found to be markedly superior to the others (*3*). Thereafter in the studies of the general population, three plates per specimen were used, including two of a highly selective medium. S. S. agar became available in 1940 and thereafter was used instead of one plate of the desoxycholate citrate agar (*1*). One of the two highly selective media was utilized almost exclusively for institutional inmates, usually one plate per culture. The efficacy of the cultural tests was improved only slightly by the changes following 1937 and the laboratory findings for these years are considered to be comparable.

One thousand four hundred and ninety-nine cases of diarrheal diseases in the general population were studied, excluding those seen in 1936 and those in Puerto Rico. Satisfactory clinical data were obtained on 1,247 of these, and epidemiological histories on 830 households. There were, in addition, 8,643 survey examinations. Cultures on institutional inmates now number in excess of 100,000 and among these proved infection and clinical disease were relatively common.

OBSERVATIONS IN NEW MEXICO, GEORGIA, AND NEW YORK

For the analysis of data relative to etiology, the cases were divided by clinical diagnosis, severity of illness, and time, in relation to onset, of the first cultural examination. There were 1,268 cases of "primary diarrhea." The remaining 231, designated here as "other diarrheal disorders," include cases in which the diarrhea occurred as a symptom or as an intercurrent infection in the course of some other major disturbance, groups of cases having the typical characteristics of staphy-

lococcal or other "food poisoning," epidemic diarrhea of the newborn, and chronic diarrheal disease clinically diagnosed as ulcerative colitis or tuberculous enteritis. The classification by severity which was recorded on the histories was fatal, severe (nonfatal), moderate, and mild. The first two and the last two are combined in certain of the tables, giving two groups which are designated "severe" and "milder" disorders. The few cases with severity unspecified were included in the second group. A consideration of the stage of the disease at the time of first examination is of particular importance in this series, since less than one-half (47 percent) of the cases were cultured before the beginning of convalescence.

It is known that repeated examinations increase the percentage of proved positive cases (*4, 5*). Our findings relative to the significance of single and multiple tests are shown in table 1. There was an increase in the proportion of positive cases as the number of examinations increased. For the severe cases this varied from 62 percent positive in those with one examination to 90 percent in those with more than three examinations; for all cases the corresponding increase was from 56 to 85 percent, respectively. The difference in the clinical character of the cases probably contributed to this variation since in prolonged illness it was easier to obtain multiple specimens during the acute phase.

TABLE 1.—*The prevalence of* Shigella paradysenteriae *infections discovered by examinations during illness in individuals with primary acute diarrhea by number of examinations and severity of disease*

Number of examinations during illness	Severe			Milder			Total		
	Cases	Positive		Cases	Positive		Cases	Positive	
		Number	Percent		Number	Percent		Number	Percent
1	61	38	62	148	80	54	209	118	56
2	56	40	71	54	35	65	110	75	68
3	74	58	78	43	23	54	117	81	69
4 or more	58	52	90	23	17	74	81	69	85
Total	249	188	76	268	155	58	517	343	66

The findings on the New Mexico and Georgia "primary" cases examined during illness are shown in the first columns of table 2. For all ages 76 percent of the severe and 58 percent of the milder cases were culturally positive. The true proportions are presumably higher since in the negative cases 38 percent of the severe and 60 percent of the milder ones had only one examination during illness.

The second part of table 2 gives the observations on the cases which were examined first during convalescence or after recovery. For all ages, 58 percent of the severe and 32 percent of the milder cases were positive for *Shigella*. The totals for all cases irrespective of the time

TABLE 2.—*The discovered prevalence of* Shigella paradysenteriae *infection in individuals with primary acute diarrhea by location, time of first examination, severity of illness, and age of individuals*

Age	New Mexico and Georgia cases																									New York City cases		
	First examined during acute phase of illness									First examined in convalescence or after recovery									Total									
	Severe			Milder			Total			Severe			Milder			Total			Severe			Milder			Grand total			Grand total		
		Positive			Positive			Positive			Positive			Positive			Positive			Positive			Positive			Positive			Positive	
	Cases	Number	Percent	Cases	Number	Percent	Cases	Number	Percent	Cases	Number	Percent	Cases	Number	Percent	Cases	Number	Percent	Cases	Number	Percent	Cases	Number	Percent	Cases	Number	Percent	Cases	Number	Percent
Under 6 months	41	26	63	27	9	33	68	35	52	0	0	0	36	5	14	36	5	14	41	26	63	63	14	22	104	40	38	57	4	7
6–12 months	45	31	69	44	23	52	89	54	61	16	11	69	41	13	32	57	24	42	61	42	69	85	36	42	146	78	53	21	4	19
1 year	55	43	78	56	37	66	111	80	72	20	14	70	80	30	38	100	44	44	75	57	76	136	67	49	211	124	59	27	9	33
2 years	19	18	95	36	24	67	55	42	76	14	10	71	45	21	47	59	31	53	33	28	85	81	45	56	114	73	64	16	10	63
3 years	9	8	89	16	10	63	25	18	72	1	1	100	22	9	41	23	10	44	10	9	90	38	19	50	48	28	58	13	7	54
4 years	2	2	100	9	8	89	11	10	91	3	2	67	18	6	33	21	8	38	5	4	80	27	14	52	32	18	56	9	9	100
5–9 years	6	6	100	21	14	67	27	20	74	3	1	33	33	12	36	36	13	36	9	7	78	54	26	48	63	33	52	27	21	78
10–14 years	3	3	100	1	1	100	4	4	100	6	3	50	29	7	24	35	10	29	9	6	67	30	8	27	39	14	36	10	7	70
15–24 years	17	13	76	13	7	54	30	20	67	9	3	33	55	22	40	64	25	39	26	16	62	68	29	43	94	45	48	2	2	100
25–34 years	20	15	75	19	13	68	39	28	72	11	5	45	35	8	23	46	13	28	31	20	65	54	21	39	85	41	48	3	2	67
35–44 years	12	9	75	11	5	45	23	14	61	11	4	36	29	3	10	40	7	18	23	13	67	40	8	20	63	21	33	2	1	50
45–54 years	8	4	67	6	1	17	14	5	36	8	7	88	17	6	35	25	13	52	16	11	69	23	7	30	39	18	46	0	0	0
55+years	10	8	80	5	1	20	15	9	60	2	0	0	8	5	63	10	5	50	12	8	67	13	6	46	25	14	56	3	2	67
Unknown	2	2	100	4	2	50	6	4	67	1	0	0	7	0	0	8	0	0	3	2	67	11	2	18	14	4	29	1	0	0
Total	249	188	76	268	155	58	517	343	66	105	61	58	455	147	32	560	208	37	354	249	70	723	302	42	1,077	551	51	191	78	41

during or following the disease of the first examination are given in the third part of the table. We examined 1,077 cases of acute primary diarrhea in New Mexico and Georgia and found 551 (51 percent) culturally positive for *Shigella paradysenteriae*. The last section of the table records the observations on New York City cases which were predominantly mild disorders; 78 (41 percent) of the 191 cases were culturally positive.

Within each of the groups the observations are arranged according to the ages of the individuals tested. In general the percentage of positive cases was lowest at ages under 6 months. It was higher at 6 to 12 months and still higher for those in the second year of life. Above this the percentages were generally high. There were variations by locality and severity of illness. Sixty-three percent of the severe diarrheal diseases in New Mexico and Georgia infants under 6 months old were culturally positive for *Shigella;* 33 percent of the mild disorders examined during the acute phase of the illness were positive. In New York City, *Shigella* infection in young infants was rare; 57 cases were studied and only 4 (7 percent) were culturally positive. Corresponding variations, though less marked, were observed at ages 6 to 12 months and during the second year of life. Beyond this, however, the percentages of positives were as high in New York City as in New Mexico and Georgia.

TABLE 3.—*The discovered prevalence of* Shigella *infections in acute primary and in other diarrheal disorders by severity of illness*

Severity	Acute primary diarrheal disorders						Other diarrheal disorders						Grand total		
	New Mexico and Georgia			New York			New Mexico and Georgia			New York				Positive	
	Cases	Positive		Cases	Positive		Cases	Positive		Cases	Positive		Cases		
		Number	Percent		Number	Percent		Number	Percent		Number	Percent		Number	Percent
Mild	305	110	36	109	37	34	51	6	12	58	3	5	523	156	30
Moderate	302	172	49	57	31	54	29	3	10	17	0	0	455	206	45
Severe	288	201	70	22	9	41	31	5	16	2	0	0	343	215	63
Fatal	66	48	73	1	0	0	12	3	25	7	1	14	86	52	61
Unspecified	66	20	31	2	1	50	17	6	35	3	0	0	92	27	29
Total	1,077	551	51	191	78	41	140	23	16	91	4	.5	1,499	656	44

The cultural findings by severity of the illness in the "acute primary" and "other" diarrheal disorders are given in table 3. The proportion found positive increased with the severity of the illness. Of the positive cultures obtained from cases not classified as primary, it is likely that some were cases with two diseases occurring concurrently, while others were passive carriers of *Shigella* ill from some

other cause. In still others, clinical classification may have been in error. The importance of each of these factors is related to the general prevalence of *Shigella* infection in each area.

The varieties and types of *Shigella* isolated from cases are listed in table 4. The outstanding difference by areas was the preponderance of Sonne and the rarity of Newcastle in New York as compared with New Mexico and Georgia. Flexner "W" was more commonly encountered than other members of the Flexner group. Multiple infections discovered concurrently were not unusual in New Mexico. In 2 years 514 *Shigella* infections were found in 495 cases.

TABLE 4.—*The varieties and strains of* Shigella *isolated in the different areas and years*

Variety of *Shigella*	New Mexico, 1937		New Mexico, 1938		Georgia, 1939–40		New York, 1939–40	
	Cases positive	Percent of total	Cases positive	Percent of total	Cases positive	Percent of total	Cases positive	Percent of total
Flexner V	7	3	19	6	13	16	0	0
W	57	28	144	47	18	23	11	14
Z	46	23	23	7	10	13	4	5
Not classified	19	9	1	(1)	2	2	13	16
Flexner—total	129	63	187	61	43	54	28	35
Sonne	52	25	64	21	18	22	46	57
"Newcastle"	24	12	58	19	17	22	1	1
Shiga	0	0	0	0	1	1	0	0
Schmitz	0	0	0	0	0	0	6	7
Total	205	100	309	100	79	100	81	100

[1] Less than 0.5.

Pathogenic organisms other than *Shigellae* were encountered very rarely. Two endemic cases were proved to be due to *Salmonellae*, one in a laboratory worker having contact with known infected animals. *Eberthella typhosa* was isolated from two children considered to be suffering from diarrhea and enteritis. Cases suggesting amebic dysentery were examined but trophozoites were observed in only one clinical case in New Mexico, even though, as previously reported by Spector and Hardy (*6*), there was a high prevalence of *Endamoeba histolytica* cyst carriers.

Bacteriologically and protozoologically negative cases were often encountered in which the epidemiological observations indicated a communicable disease. It seemed possible that pathogens as yet unidentified might be responsible. In this connection we gave particular attention to the substantial number of Gram-negative bacilli which gave a "*Salmonella* reaction" on Krumwiede's medium. Most of these formed indol, a very few liquefied gelatin, the Voges-Proskauer reaction was negative, and the methyl-red positive. Lactose was often fermented from the fifth to the twenty-first day; sucrose was utilized more frequently and earlier (rarely before the third day). The action on other carbohydrates varied. We did not encounter any distinct cultural or

serological grouping. Such "*Salmonella*-like" organisms were frequently isolated from specimens collected from groups with a high incidence of diarrheal disease, whereas they were rarely found in cultures obtained in areas or institutional groups where acute diarrhea was unusual. This relation in occurrence and nonoccurrence justifies the suspicion that these organisms might have an etiological role in diarrheal disorders, but we have no other evidence either to support or refute this hypothesis.

FINDINGS IN PUERTO RICO

In Puerto Rico there were unanticipated obstacles to the collection of data comparable to those from the other three areas. Despite the exceptionally high reported mortality from diarrhea and enteritis, we failed to find a method of reaching a significant number of severe cases before death. An examination of death certificates revealed that only a small percentage of these fatal illnesses in children were seen by any physician prior to death. A group of cases was examined by rectal swab cultures obtained after death. The findings indicated a high mortality from *Shigella* infections but failed to provide adequate evidence as to the various etiological factors involved.

BACTERIOLOGICAL STUDIES OF INSTITUTIONAL INMATES

Examination was made of cases of diarrhea occurring among the inmates of various institutions. Two groups were studied more intensively than others. The findings already reported (*7, 8*) which relate to the present subject were as follows: In a New York State institution, among an average of 123 boys and 120 girls, there were 194 attacks of acute diarrhea in 20 months; 100 (52 percent) of these were culturally positive for *Shigella*. It was clearly evident that there was a variety of mild diarrhea which was culturally negative, while most of the cases of severe acute illness were found positive for *Shigella*. In the Puerto Rican Mental Hospital, during a 4-month period, 105 cases of diarrhea occurred; 77 (73 percent) were found positive for *Shigella*. Subsequent to the published reports, 93 additional cases occurring in this hospital were cultured; 72 (77 percent) were positive.

EPIDEMIC DIARRHEAL DISORDERS

As a part of our studies we investigated 23 epidemics of diarrheal disease. ("Epidemic" and "outbreak" are used synonymously for a prevalence of disease significantly greater than the norm for the affected group.) Nine were explosive, 13 nonexplosive, and 1 was mixed.

In seven of the explosive outbreaks, the epidemic and the individual cases had a sudden onset and a brief though stormy course. There

were no secondary cases. Gram-negative pathogenic bacilli were not found on fecal cultures. These were typical food-poisoning outbreaks.

The other two explosive epidemics were due to *Shigella* ("Newcastle") and *Salmonella typhi murium*, respectively. In these the primary cases appeared throughout 1 week, though chiefly within 3 days. Secondary cases were found. The usual duration of illness was 2 to 5 days, though there were a few transient disorders and some prolonged disturbances. Clinically, the cases were clearly differentiated from those in the food-poisoning outbreaks, and stool cultures were positive.

The nonexplosive outbreaks were widely scattered, three in military camps, three in civilian groups, and seven among the inmates of mental institutions. Preceding the epidemics, cases of diarrheal diseases had occurred only sporadically. The unusual incidence began insidiously, increased gradually, and was maintained persistently. The cases varied in severity and duration. In all instances these outbreaks were found to be due to some single variety of *Shigella paradysenteriae*. The mixed epidemic was an explosive "food poisoning" outbreak, superimposed on a nonexplosive *Shigella* epidemic.

SUMMARY

The acute diarrheal diseases were studied in four widely separated regions. Both bacillary and protozoan causes of these disorders were sought and attention was given to the study of organisms not previously described as pathogenic. The newer highly selective culture media for *Shigella* were employed for the bacteriological examinations.

In all areas investigated the *Shigella paradysenteriae* group was found most commonly in these diseases. No other recognized pathogen was identified in a significant proportion of the cases studied.

The relative importance of *Shigellae* as causative agents varied according to the age of the patient, the locality involved, and the severity of the illness. *Shigellae* were isolated from an increasing percentage of cases with increasing age up to the third year of life. Thereafter the percentage remained relatively constant and uniform in all areas. Under 2 years of age these organisms played a lesser role in the causation of diarrheal diseases in New York than in New Mexico and Georgia. The severe cases had a higher percentage of positive observations than the milder ones.

Multiple examinations increased the percentage of positive findings. Examination during the acute phase of the disease revealed a higher proportion of positive cases than was found in those first tested in convalescence or after recovery. Reported data must be valuated with respect to these and other variables.

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THE METABOLISM OF 2,2 BIS(P-CHLOROPHENYL) 1,1,1 TRICHLOROETHANE (DDT). I. A METABOLITE FROM RABBIT URINE, DI(P-CHLOROPHENYL)ACETIC ACID; ITS ISOLATION, IDENTIFICATION, AND SYNTHESIS [1]

By WILLIAM C. WHITE, *Assistant Physicist*, and THOMAS R. SWEENEY, *Assistant Chemist*

INTRODUCTION

It has been pointed out that DDT is toxic to experimental animals when ingested in relatively large amounts (*1, 2, 3, 4, 5*). In the toxicological studies of DDT it became desirable to gain some knowledge of its metabolic fate. The purpose of this paper is to describe the isolation and identification of one metabolic product present in the urine of rabbits following the ingestion of DDT in olive oil solution and, from a study of the degradation of DDT in vitro, to suggest a possible mechanism for its formation.

In the development of this work two of the principal techniques used were X-ray powder diffraction analysis and quantitative determination of organic chlorine. In many instances, X-ray powder diffraction gives a qualitative analysis of a mixture which would be impossible or quite difficult to obtain using the usual laboratory procedures. The organic chlorine was determined by the method of Winter (*6*) as modified by Fleck (*7*).

The urine from rabbits exposed to DDT in a manner to be described showed the presence of a considerable amount of organic chlorine,

[1] From the Industrial Hygiene Research Laboratory, National Institute of Health.

whereas negative tests were obtained from normal rabbit urine. Furthermore, X-ray diffraction patterns obtained from the residues left on evaporation of ether extracts of these urines were different. This indicated the presence of an abnormal constituent in the urine from the exposed animals. Examination of the abnormal pattern showed it to be identical with the pattern previously obtained from a compound believed to be di(p-chlorophenyl)acetic acid.[2] (See fig. 1.)

Proof that the metabolite was, in fact, di(p-chlorophenyl)acetic acid was obtained by isolation of the compound from urine and comparison with a synthesized sample of the compound with respect to chemical analyses, melting points, mixed melting points, and X-ray powder diffraction analyses.

EXPERIMENTAL

Eight rabbits of either sex weighing between 2 and 3 kg. and feeding on the stock laboratory diet ad libitum were used. A dose of 100 mg. of DDT per kg. body weight was given to each rabbit 6 days a week and was administered in olive oil solution by means of a stomach tube. The solution contained 50 mg. of pure DDT (melting point 107°–108° C.) per ml. of olive oil. The urine was collected daily and was kept refrigerated without preservative.

ISOLATION OF DI(P-CHLOROPHENYL)ACETIC ACID FROM URINE

Quantitive determination of the organic chlorine was used as a guide in the study of the isolation of the metabolite from urine. In this way it was possible to follow the distribution of the compound through various trial fractionations.

The urine from the rabbits exposed to DDT was combined and filtered. It was acidified to a pH of 2 or lower with dilute sulfuric acid and heated to 80°–90° C. for an hour.[3] After cooling, the urine was extracted several times with one-third its volume of ether. Emulsions, if formed, were broken by stirring with anhydrous sodium sulfate. The ether extracts were combined and extracted three times with a 5-percent solution of either sodium or potassium hydroxide. Determination of organic chlorine at this point showed that 83 percent of the organic chlorine present in the original ether extracts had been extracted by the alkali. The alkaline extract was washed once with ether and brought to a pH of 2 or lower with dilute sulfuric acid,

[2] The X-ray powder diffraction pattern of di(p-chlorophenyl)acetic acid was first obtained from a sample kindly supplied by S. A. Hall, U. S. Department of Agriculture, Beltsville Research Center, Beltsville, Md., who prepared it by the hydrolysis of DDT with potassium hydroxide in ethylene glycol. The structure was suggested by Dr. Hall but had not been confirmed at that time.

[3] This was done in order to hydrolyze any conjugated derivatives of the metabolite. The type of conjugation, if any, was not determined, but certainly a large portion of it is excreted as a simple salt or in a very easily hydrolyzed form, since good yields were obtained by acidification without heating.

whereupon a copious precipitate appeared. The mixture was extracted twice with ether and the ether extract washed several times with water in order to free it of sulfuric acid. The ether extract was then allowed to evaporate, yielding a dark-brown syrup which partially crystallized on standing in a dessicator over sulfuric acid for a few days. The X-ray powder diffraction pattern of di(p-chlorophenyl)-acetic acid was obtained from this residue. The residue was boiled for a few minutes with a small quantity of carbon tetrachloride and cooled. After cooling, the dark, gummy material coagulated on the bottom and sides of the beaker from which the moderately colored carbon tetrachloride was decanted. This extraction was repeated three or four times. The combined carbon tetrachloride extracts were treated with decolorizing carbon and reduced to a small volume. On scratching the sides of the beaker, di(p-chlorophenyl)acetic acid crystallized in small, rectangular prisms. The crystals were filtered and washed with a small amount of carbon tetrachloride. The product was recrystallized three times from dilute alcohol; melting point 166°–166.5° C. (uncorrected). The analyses and comparison with the synthesized compound are shown in table 1.

SYNTHESIS OF DI(P-CHLOROPHENYL)ACETIC ACID

Although the product obtained from the degradation of DDT, in a manner to be described subsequently, was identified, with reasonable certainty, as di(p-chlorophenyl)acetic acid, it was desired to confirm this identity by an independent synthesis. This was accomplished by condensing chlorobenzene with glyoxylic acid.

Glyoxylic acid was prepared by the reduction of oxalic acid with sodium-zinc amalgam according to a method of Mohrschulz (*8*). The glyoxylic acid was not crystallized but was used as a syrup. A strong Hopkins-Cole reaction (*9*) with indole was obtained from a drop of this syrup.

To 3 gm. of the crude yield of glyoxylic acid monohydrate was added 12 gm. of monochlorobenzene. The mixture was cooled to 10° C. and 15 ml. of concentrated sulfuric acid was added with vigorous stirring at such a rate that the temperature did not rise above 20° C. After addition of the concentrated sulfuric acid, 1.5 ml. of fuming sulfuric acid was added with continued stirring. After 5 minutes the reaction mixture was poured over cracked ice and diluted with about 10 volumes of water. The mixture was extracted twice with 100-ml. portions of ether and the combined ether extracts washed with water. The ether solution was extracted several times with 5-percent potassium hydroxide and the alkaline extract was then acidified with hydrochloric acid, whereupon the di(p-chlorophenyl)-acetic acid precipitated. The yield of crude product was 18.6 percent

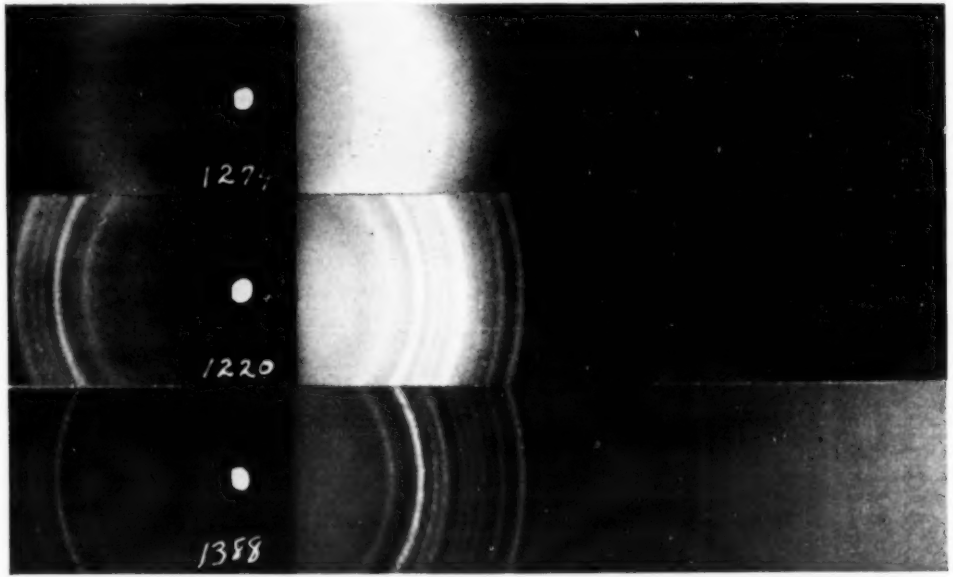


FIGURE 1.—Comparison of X-ray powder diffraction patterns from normal rabbit urine (1274), urine of rabbits exposed to DDT (1220), and pure di(p-chlorophenyl)acetic acid (1388).

TABLE 1.—*Comparison of di(p-chlorophenyl)acetic acid obtained from urine of rabbits exposed to DDT, from the condensation of glyoxylic acid and chlorobenzene, and from the degradation of DDT*

Acid obtained from—	Melting point (uncorrected)	Mixed melting point	Analyses[1]			X-ray powder diffraction pattern
			C	H	Cl	
Urine of exposed rabbits	166–166.5° C.	No change	59.54 59.69	3.68 3.70	25.37	1315
Glyoxylic acid and chlorobenzene	165–166° C.	No change	59.76	3.68	25.07	1358
Degradation of DDT	166–166.5° C.	No change	----	----	----	1397
Theoretical	----	----	59.85	3.59	25.33	

[1] For the microanalyses the authors are indebted to Dr. A. T. Ness, Chemistry Laboratory, National Institute of Health.

of the theoretical based on the glyoxylic acid used. After two recrystallizations from dilute alcohol the melting point was 165°–166° C. The analyses are given in table 1 and the X-ray powder diffraction data in table 2.

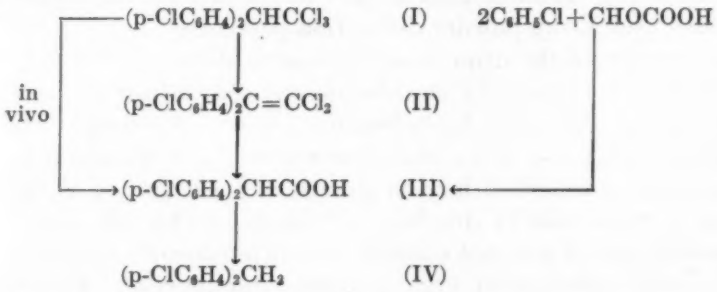
TABLE 2.—*X-ray powder diffraction data for di(p-chlorophenyl)acetic acid*

d	$\frac{I}{I_0}$ [1]	d	$\frac{I}{I_0}$
13.3	0.07	2.89	0.07
5.66	.33	2.80	.08
4.73	1.00	2.66	.13
4.38	.53	2.55	.13
4.18	.45	2.47	.05
3.84	.28	2.39	.07
3.70	.30	2.28	.06
3.54	.27	2.18	.07
3.40	.17	2.14	.12
3.28	.38	2.10	.03
3.18	.05	2.06	.05
3.06	.57	1.90	.12
2.96	.03		

[1] $Cu_{K\text{-}alpha}$ radiation.

DEGRADATION OF DDT IN VITRO

In an attempt to throw some light on the mechanisms of the transformations of DDT in vivo, the degradation of DDT in vitro was studied in some detail. It was found that by varying the severity of treatment, DDT (I) could be degraded stepwise through 2,2 bis(p-chlorophenyl) 1,1 dichloroethylene (II), di(p-chlorophenyl)acetic acid (III), and finally to 4,4′ dichlorodiphenylmethane (IV).



2,2 bis(p-chlorophenyl) 1,1 dichloroethylene (II).—By heating DDT with an excess of potassium hydroxide in alcoholic solution for 15 to 20 minutes, II was prepared in almost quantitative yields (*10*).

Di(p-chlorophenyl)acetic acid (III).—To 10 gm. of either I or II were added 25 gm. of barium hydroxide octahydrate (excess) and 250 ml. of ethylene glycol. The mixture was refluxed for 10 to 12 hours at a temperature between 160° and 170° C. After cooling, the reaction mixture was diluted with an equal volume of water, made acid to Congo with hydrochloric acid, and extracted twice with ether. The

ethereal solution was extracted several times with 5-percent potassium hydroxide solution and the alkaline extract washed once with ether. Acidification of the alkaline solution precipitated III, which was purified by redissolving in dilute potassium hydroxide, filtering, and reprecipitating. The acid was recrystallized from dilute alcohol, melting point 166° to 166.5° C. (uncorrected). The yield of crude product from I was 33 percent.

4, 4' dichlorodiphenylmethane (*IV*).—To 4 gm. of either I, II, or III in 250 ml. of ethylene glycol were added 8 gm. of potassium hydroxide and the mixture refluxed for 10 to 12 hours. The reaction mixture was then diluted with an equal volume of water and extracted twice with 100-ml. portions of ether. The ethereal extract was evaporated, usually leaving an oily liquid which was readily crystallized by scratching the beaker with a glass rod (the compound tends to become supercooled). The yield of crude product is almost quantitative. After decolorization with carbon and recrystallization from alcohol the compound melted at 55° C. The crystal form and melting point agree with the compound described by Montagne (*11*).

DISCUSSION

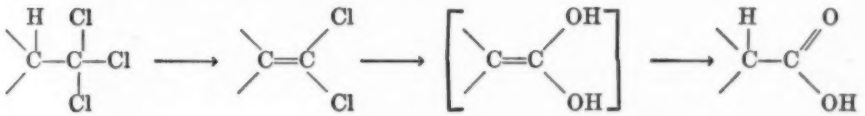
The data in table 1 show that the metabolite isolated from the urine of rabbits exposed to DDT, the product synthesized from the condensation of chlorobenzene with glyoxylic acid, and the acid prepared from DDT are identical. Further proof of this was obtained by the decarboxylation of each of the above products and a comparison of the decarboxylation products with respect to melting points, mixed melting points, and X-ray powder diffraction patterns.

Fractionation of the urine from exposed rabbits revealed that 80 to 85 percent of the total organic chlorine was concentrated in an alkali-soluble and bicarbonate-soluble fraction. Since extraction of the pure crystalline metabolite from this fraction was not quantitative, and since we have no method for the quantitative estimation of the total amount of metabolite in this fraction except by the determination of organic chlorine, it was not certain that di(p-chlorophenyl)acetic acid was the only chlorinated organic compound present. However, it would be difficult to explain the presence of a chlorinated organic acid resulting from the degradation of DDT, other than the one found, which would be acidic enough to dissolve in bicarbonate, without assuming that a carbon-to-carbon bond from a phenyl group to the methane carbon was broken or that one or both phenyl groups were cleaved in the process. The apparent stability of the dichlorodiphenylmethane structure as shown by the in vitro studies makes such drastic transformations unlikely. This indicates that the principal metabolite of DDT in rabbits is di(p-chlorophenyl)acetic acid.

The presence of unchanged DDT in the urine of exposed rabbits as assumed by Smith and Stohlman (*3*) was not verified by X-ray diffraction analyses. It was found that the X-ray powder diffraction pattern of DDT could be obtained from the residue on evaporation of an ether extract of 100 ml. of a normal rabbit urine to which 5 mg. of DDT had been added. This indicates that if any DDT is present in the urine of exposed rabbits it is in amounts less than 5 mg. percent.

It seems possible that the degradation of DDT in vivo parallels the degradation in vitro. The mechanism probably involves the following steps:

1. Dehydrohalogenation of DDT to II.
2. Hydroxylation of II with replacement of the ethylenic chlorine atoms to give the enol form of III.
3. Ketonization of the enol to yield III.



SUMMARY

DDT, when fed to rabbits, yields di(p-chlorophenyl)acetic acid in the urine. The isolation and synthesis of this metabolite are described.

The degradation of DDT in vitro is described.

A possible mechanism for the degradation of DDT in vivo is suggested.

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DEATHS DURING WEEK ENDED DECEMBER 23, 1944

[From the Weekly Mortality Index, issued by the Bureau of the Census, Department of Commerce]

	Week ended Dec. 23, 1944	Corresponding week, 1943
Data for 90 large cities of the United States:		
Total deaths	9,216	12,592
Average for 3 prior years	9,904	
Total deaths, 51 weeks of year	453,666	468,574
Deaths under 1 year of age	588	628
Average for 3 prior years	587	
Deaths under 1 year of age, 51 weeks of year	31,106	33,245
Data from industrial insurance companies:		
Policies in force	66,896,645	66,110,375
Number of death claims	12,968	12,107
Death claims per 1,000 policies in force, annual rate	10.1	9.5
Death claims per 1,000 policies, 51 weeks of year, annual rate	10.1	9.6

PREVALENCE OF DISEASE

No health department, State or local, can effectively prevent or control disease without knowledge of when, where, and under what conditions cases are occurring

UNITED STATES

REPORTS FROM STATES FOR WEEK ENDED DECEMBER 30, 1944

Summary

The incidence of meningococcus meningitis, although since February continuously lower than last year, continues the upward trend begun early in September. Of the current total of 198 cases reported, 99 occurred in the Middle Atlantic and East North Central areas, 10 in Tennessee, and 14 in California. The total for the corresponding week last year was 463, and the median for the corresponding weeks of the past 5 years (1939–43) is 37. The total for the 52 weeks of the year is 16,059, as compared with 17,922 last year and a 5-year median of 2,023.

Of the total of 75 reported cases of poliomyelitis, as compared with 89 last week and a 5-year median of 39, New York reported 30, California 9, Illinois 5, and Ohio and Washington 4 each. The total of 19,268 cases reported for the 52 weeks of the year is more than has been reported for any year since 1916, when the total was 27,363. The corresponding figure last year is 12,401, and the 5-year median is 9,056.

Of the current total of 3,749 cases of scarlet fever (more than for the corresponding week of any year since 1937), 1,735 were reported in the Middle Atlantic and East North Central areas, where 1,238 of the total of 3,021 cases for the corresponding week last year occurred.

A total of 3,466 cases of influenza was reported, of which 2,817 occurred in 3 States—Texas (2,121), South Carolina (417), and Virginia (279). For the corresponding week last year a total of 126,488 cases was reported, and the 5-year median is 7,097. The cumulative total for the 52 weeks of the year is 367,868, as compared with 421,155 last year and a 5-year median of 309,669.

Deaths registered during the week in 93 large cities of the United States totaled 9,934, as compared with 9,305 last week, a 3-year (1941–43) average of 11,287, and 14,427 for the corresponding week last year. The cumulative total for the 52 weeks of the year is 468,769, as compared with 487,931 for the corresponding 52 weeks last year.

Telegraphic morbidity reports from State health officers for the week ended December 30, 1944, and comparison with corresponding week of 1943 and 5-year median

In these tables a zero indicates a definite report, while leaders imply that, although none was reported, cases may have occurred.

Division and State	Diphtheria			Influenza			Measles			Meningitis, meningococcus		
	Week ended—		Median 1939–43	Week ended—		Median 1939–43	Week ended—		Median 1939–43	Week ended—		Median 1939–43
	Dec. 30, 1944	Jan. 1, 1944		Dec. 30, 1944	Jan. 1, 1944		Dec. 30, 1944	Jan. 1, 1944		Dec. 30, 1944	Jan. 1, 1944	
NEW ENGLAND												
Maine	0	0	0	-	87	1	4	184	39	0	3	0
New Hampshire	0	0	0	-	-	-	0	1	6	0	0	0
Vermont	0	0	0	7	189	-	0	13	24	0	0	0
Massachusetts	8	21	2	-	-	-	61	262	223	6	18	3
Rhode Island	1	0	0	21	60	-	0	106	26	0	4	1
Connecticut	0	1	0	-	683	1	20	9	67	2	7	2
MIDDLE ATLANTIC												
New York	14	11	14	[1] 3	[1] 199	[1] 15	57	542	542	29	65	5
New Jersey	4	2	9	5	270	17	17	437	150	12	23	3
Pennsylvania	14	9	15	1	57	-	28	516	533	13	45	10
EAST NORTH CENTRAL												
Ohio	5	6	10	3	8,037	45	9	1,130	47	7	21	4
Indiana	16	3	10	11	117	37	6	126	32	6	8	0
Illinois	8	5	24	11	361	24	18	86	84	16	36	2
Michigan [3]	11	10	6	2	294	6	11	968	172	10	38	2
Wisconsin	5	3	1	11	2,323	44	17	419	217	6	5	1
WEST NORTH CENTRAL												
Minnesota	4	10	1	1	18	-	71	268	67	3	8	0
Iowa	4	1	2	-	4,377	10	11	40	56	2	7	1
Missouri	3	1	2	7	68	5	3	18	11	6	16	1
North Dakota	7	2	2	3	595	24	0	329	16	0	2	0
South Dakota	1	6	2	-	1	1	0	80	4	0	2	0
Nebraska	1	7	0	5	393	-	8	5	5	0	3	0
Kansas	4	11	6	-	2,195	26	15	23	64	1	7	1
SOUTH ATLANTIC												
Delaware	1	0	0	-	-	-	5	4	4	1	1	0
Maryland [3]	10	3	3	1	586	7	4	72	9	2	12	2
District of Columbia	0	1	1	1	603	5	0	39	4	3	6	1
Virginia	10	1	30	279	9,690	432	16	409	103	6	7	3
West Virginia	1	2	6	15	12,068	18	4	98	16	0	0	1
North Carolina	14	4	14	7	223	26	15	300	136	3	5	1
South Carolina	2	10	10	417	6,155	674	4	79	45	0	3	1
Georgia	3	5	10	20	6,513	636	0	125	25	1	7	1
Florida	3	5	5	2	140	22	0	26	2	1	7	0
EAST SOUTH CENTRAL												
Kentucky	4	7	6	7	20,491	25	0	8	32	4	7	3
Tennessee	7	6	6	47	1,753	61	70	66	66	10	5	0
Alabama	14	6	13	71	7,022	332	4	140	15	6	2	3
Mississippi [3]	7	4	8	-	-	-	-	-	-	3	3	0
WEST SOUTH CENTRAL												
Arkansas	4	6	12	126	5,345	108	8	22	34	3	4	0
Louisiana	7	2	8	6	4,136	10	9	1	3	6	7	2
Oklahoma	8	8	14	71	2,875	126	3	0	4	0	7	0
Texas	56	31	40	2,121	13,330	1,254	71	66	66	9	4	3
MOUNTAIN												
Montana	7	4	1	-	2,521	192	3	134	41	1	3	0
Idaho	0	0	0	1	29	2	1	3	4	0	0	0
Wyoming	0	0	0	18	952	115	3	13	2	0	0	0
Colorado	2	6	6	25	808	145	6	188	59	0	2	0
New Mexico	1	0	1	1	81	9	0	0	6	0	2	0
Arizona	0	0	2	109	824	157	4	26	26	2	3	0
Utah [3]	0	0	0	-	1,767	964	10	3	48	0	1	0
Nevada	0	0	0	-	792	-	3	0	0	0	0	0
PACIFIC												
Washington	21	4	3	-	220	3	18	43	43	2	8	1
Oregon	7	4	3	14	2,811	171	37	55	55	2	4	0
California	32	27	19	15	4,429	60	237	168	168	14	35	2
Total	331	255	323	3,466	126,488	7,097	891	7,650	5,786	198	463	37
52 weeks	[2] 14,103	13,744	15,715	367,868	421,155	309,669	602,397	602,085	505,871	16,059	17,922	2,023

[1] New York City only.
[2] Cumulative totals changed by corrected reports.
[3] Period ended earlier than Saturday.

Telegraphic morbidity reports from State health officers for the week ended December 30, 1944, and comparison with corresponding week of 1943 and 5-year median—Con.

Division and State	Poliomyelitis			Scarlet fever			Smallpox			Typhoid and paratyphoid fever [2]		
	Week ended—		Median 1939–43	Week ended—		Median 1939–43	Week ended—		Median 1939–43	Week ended—		Median 1939–43
	Dec. 30, 1944	Jan. 1, 1944		Dec. 30, 1944	Jan. 1, 1944		Dec. 30, 1944	Jan. 1, 1944		Dec. 30, 1944	Jan. 1, 1944	
NEW ENGLAND												
Maine	0	0	0	58	22	12	0	0	0	1	1	0
New Hampshire	1	0	0	20	4	4	0	0	0	0	0	0
Vermont	0	0	0	6	14	8	0	0	0	0	0	0
Massachusetts	0	2	1	251	246	196	0	0	0	2	2	2
Rhode Island	0	0	0	17	4	4	0	0	0	0	0	0
Connecticut	0	0	0	61	34	29	0	0	0	0	0	0
MIDDLE ATLANTIC												
New York	30	2	2	406	252	285	0	0	0	2	1	4
New Jersey	1	1	1	109	84	95	0	0	0	0	2	1
Pennsylvania	0	0	0	251	213	180	0	0	0	3	1	6
EAST NORTH CENTRAL												
Ohio	4	0	1	242	212	225	0	0	0	2	5	5
Indiana	0	0	0	144	48	117	0	0	1	1	0	0
Illinois	5	5	3	255	160	182	0	0	1	0	1	2
Michigan [3]	0	1	1	214	160	160	0	0	0	2	2	2
Wisconsin	3	8	1	114	109	124	2	0	0	1	1	0
WEST NORTH CENTRAL												
Minnesota	0	0	1	62	85	68	0	0	5	1	0	0
Iowa	2	0	2	64	62	62	0	0	1	0	0	0
Missouri	3	1	0	69	45	46	0	0	0	0	0	1
North Dakota	2	1	0	11	9	12	1	0	0	0	0	0
South Dakota	0	0	0	10	30	22	0	0	0	1	0	0
Nebraska	0	0	0	34	47	19	0	0	0	0	1	0
Kansas	1	1	1	111	80	65	0	2	0	1	0	0
SOUTH ATLANTIC												
Delaware	0	0	0	3	1	7	0	0	0	0	1	0
Maryland [3]	1	2	0	117	57	53	0	0	0	3	2	3
District of Columbia	0	0	0	60	31	16	0	0	0	0	1	1
Virginia	0	0	0	80	50	50	0	0	0	2	2	5
West Virginia	1	0	1	28	46	51	0	0	0	0	0	1
North Carolina	0	1	0	48	49	49	0	0	0	0	0	0
South Carolina	1	0	0	5	10	10	0	0	0	1	0	0
Georgia	0	0	0	17	22	22	0	0	0	0	3	2
Florida	0	0	0	1	9	10	0	0	0	0	4	1
EAST SOUTH CENTRAL												
Kentucky	1	0	1	51	54	53	0	0	0	0	82	2
Tennessee	1	0	0	83	19	22	0	0	0	0	1	1
Alabama	1	0	0	11	9	25	0	0	0	2	1	1
Mississippi [3]	2	1	1	41	7	8	0	0	0	1	0	0
WEST SOUTH CENTRAL												
Arkansas	0	1	0	22	8	8	1	0	1	0	3	2
Louisiana	0	1	0	17	7	8	0	0	0	0	2	5
Oklahoma	0	2	1	21	69	23	1	1	1	2	1	1
Texas	0	2	2	94	37	51	0	0	4	8	0	6
MOUNTAIN												
Montana	0	0	0	13	24	23	0	0	0	0	0	0
Idaho	1	0	0	40	47	13	0	0	0	0	1	0
Wyoming	0	0	0	10	3	4	0	0	0	0	0	0
Colorado	0	1	1	57	19	21	0	0	0	0	0	1
New Mexico	1	0	0	23	10	10	0	0	0	0	3	3
Arizona	0	0	0	14	20	8	0	0	1	0	0	0
Utah [3]	1	0	1	41	94	13	0	0	0	0	0	0
Nevada	0	0	0	2	0	0	0	0	0	0	0	0
PACIFIC												
Washington	4	1	1	65	150	42	0	0	0	2	1	0
Oregon	0	1	1	26	67	9	0	0	0	1	3	0
California	9	7	2	260	182	116	0	0	0	4	0	2
Total	76	42	39	3,759	3,021	2,858	5	3	61	43	128	80
52 weeks	[4]9,270	12,401	9,056	190,316	140,475	140,475	390	733	1,368	5,392	5,546	8,513

[2] Period ended earlier than Saturday.
[3] Including paratyphoid fever reported separately as follows: Michigan, 1; Minnesota, 1; Texas, 1; Washington, 1; California, 1.
[4] Cumulative total changed by corrected reports.

Telegraphic morbidity reports from State health officers for the week ended December 30, 1944, and comparison with corresponding week of 1943 and 5-year median—Con.

Division and State	Whooping cough			Week ended December 30, 1944								
	Week ended		Median 1939–43	Anthrax	Dysentery			Encephalitis, infectious	Leprosy	Rocky Mt. spotted fever	Tularemia	Typhus fever
	Dec. 30, 1944	Jan. 1, 1944			Amebic	Bacillary	Unspecified					
NEW ENGLAND												
Maine	21	3	23	0	0	0	0	0	0	0	0	0
New Hampshire	7	0	1	0	0	0	0	0	0	0	0	0
Vermont	34	15	17	0	0	0	0	0	0	0	0	0
Massachusetts	94	50	125	0	0	3	0	1	0	0	0	0
Rhode Island	0	8	8	0	0	1	0	0	0	0	0	0
Connecticut	71	17	38	0	0	0	0	0	0	0	0	0
MIDDLE ATLANTIC												
New York	206	116	349	0	0	4		1	0	0	1	0
New Jersey	65	48	116	0	3	0	0	0	0	0	0	0
Pennsylvania	153	57	188	0	0	0	0	1	0	0	0	0
EAST NORTH CENTRAL												
Ohio	87	39	151	0	0	0	0	0	0	0	2	0
Indiana	15	6	14	0	0	0	1	0	0	0	5	0
Illinois	51	38	120	0	3	2	0	2	0	0	20	0
Michigan [2]	55	70	163	0	0	1	0	0	0	0	0	0
Wisconsin	67	62	116	0	0	0	0	0	0	0	0	0
WEST NORTH CENTRAL												
Minnesota	15	16	30	0	3	0	0	0	0	0	0	0
Iowa	12	16	22	0	0	0	0	0	0	0	0	0
Missouri	20	8	8	0	0	0	2	1	0	0	0	0
North Dakota	4	2	2	0	0	0	0	1	0	0	0	0
South Dakota	12	0	1	0	0	0	0	0	0	0	0	0
Nebraska	0	9	2	0	0	0	0	0	0	0	0	0
Kansas	28	12	28	0	0	0	0	0	0	0	1	0
SOUTH ATLANTIC												
Delaware	9	0	2	0	0	0	0	0	0	0	0	0
Maryland [2]	61	28	46	0	0	0	0	0	0	0	2	0
District of Columbia	2	3	11	0	0	0	0	0	0	0	0	0
Virginia	33	95	36	0	0	0	38	0	0	0	2	1
West Virginia	10	29	13	0	0	0	0	0	0	0	0	0
North Carolina	35	62	76	0	0	0	0	0	0	1	0	7
South Carolina	23	102	33	0	0	7	0	0	0	0	0	4
Georgia	2	25	4	0	1	0	0	0	0	0	1	16
Florida	1	19	6	0	3	0	0	0	0	0	0	3
EAST SOUTH CENTRAL												
Kentucky	8	24	39	0	0	0	0	0	0	0	7	0
Tennessee	31	9	19	0	0	0	0	0	0	0	3	5
Alabama	4	14	21	0	3	0	0	0	0	0	0	17
Mississippi [2]				0	0	0	0	0	0	0	0	3
WEST SOUTH CENTRAL												
Arkansas	23	21	15	0	0	4	0	1	0	0	1	1
Louisiana	0	0	3	0	1	0	0	0	0	0	0	1
Oklahoma	3	2	3	0	0	0	0	0	0	0	0	0
Texas	136	95	95	0	23	702	10	1	0	0	0	14
MOUNTAIN												
Montana	2	3	5	0	0	0	0	0	0	0	0	0
Idaho	1	1	2	0	0	0	0	0	0	0	0	0
Wyoming	7	3	3	0	0	0	0	0	0	0	0	0
Colorado	6	28	14	0	0	0	0	1	0	0	0	0
New Mexico	0	2	18	0	0	2	4	0	0	0	0	0
Arizona	7	20	14	0	0	0	39	0	0	0	0	0
Utah [2]	3	11	17	0	0	0	0	0	0	0	0	0
Nevada	0	0	0	0	0	0	0	0	0	0	0	0
PACIFIC												
Washington	16	34	27	0	0	0	0	0	0	0	0	0
Oregon	9	11	7	0	0	0	0	0	0	0	0	0
California	121	54	128	0	2	11	0	0	0	0	0	0
Total	1,570	1,287	2,530	0	42	737	94	10	0	1	45	72
Same week, 1943	1,287			0	25	214	234	12	0	1	18	58
Same week, 1942	2,632			0	11	95	52	16	0	0	36	67
52 weeks, 1944	95,610			40	1,899	25,032	9,126	[3] 635	32	455	719	5,337
52 weeks, 1943	176,415			65	2,129	18,182	7,621	692	30	435	808	4,533
52 weeks, 1942	177,916		[4] 176,415	78	1,195	12,043	6,431	568	45	[4] 452	922	[4] 2,940

[2] Period ended earlier than Saturday.
[3] Cumulative total changed by corrected reports.
[4] 5-year median, 1939–43.

WEEKLY REPORTS FROM CITIES

City reports for week ended December 23, 1944

This table lists the reports from 84 cities of more than 10,000 population distributed throughout the United States, and represents a cross section of the current urban incidence of the diseases included in the table.

	Diphtheria cases	Encephalitis, infectious, cases	Influenza		Measles cases	Meningitis, meningococcus, cases	Pneumonia deaths	Poliomyelitis cases	Scarlet fever cases	Smallpox cases	Typhoid and paratyphoid fever cases	Whooping cough cases
			Cases	Deaths								
NEW ENGLAND												
Maine:												
Portland	0	0	------	0	0	0	1	0	2	0	0	0
New Hampshire:												
Concord	0	0	------	0	0	0	1	0	1	0	0	0
Massachusetts:												
Boston	2	0	------	0	31	3	15	2	88	0	1	21
Fall River	0	0	------	0	0	0	2	0	5	0	0	2
Springfield	0	0	------	0	0	0	0	0	4	0	0	1
Worcester	0	0	------	0	0	0	8	0	14	0	0	14
Rhode Island:												
Providence	1	0	------	0	0	0	4	0	12	0	0	7
Connecticut:												
Bridgeport	0	0	1	1	0	0	3	0	4	0	0	0
New Haven	0	0	------	0	0	2	1	0	5	0	0	6
MIDDLE ATLANTIC												
New York:												
Buffalo	1	0	------	0	0	1	4	0	2	0	0	1
New York	10	0	1	4	4	12	45	16	165	0	3	89
Rochester	0	0	------	0	3	0	4	4	1	0	1	6
Syracuse	1	0	------	0	0	0	3	0	10	0	0	6
New Jersey:												
Camden	1	0	------	0	0	0	0	0	0	0	0	2
Newark	0	0	1	0	1	1	2	0	12	0	0	2
Trenton	0	0	------	0	0	1	1	1	5	0	0	0
Pennsylvania:												
Philadelphia	1	0	2	2	2	4	20	1	68	0	1	19
Pittsburgh	1	0	1	0	0	1	10	0	5	0	0	2
Reading	0	0	------	0	2	0	1	0	1	0	0	0
EAST NORTH CENTRAL												
Ohio:												
Cleveland	0	0	------	0	1	4	9	2	40	0	0	24
Columbus	0	0	2	2	0	1	1	0	3	0	0	3
Indiana:												
Fort Wayne	1	0	------	0	1	0	4	0	4	0	0	0
Indianapolis	2	0	------	1	2	0	8	0	21	0	0	6
South Bend	2	0	------	0	0	1	0	0	4	0	0	0
Terre Haute	0	0	------	0	0	0	2	0	7	0	0	0
Illinois:												
Chicago	1	0	2	2	4	7	19	0	85	0	0	18
Springfield	0	0	------	0	1	0	2	0	1	0	0	0
Michigan:												
Detroit	7	0	1	1	5	1	9	0	76	0	1	17
Flint	0	0	------	0	0	0	4	0	0	0	0	0
Grand Rapids	0	0	------	0	1	0	2	0	5	0	0	2
Wisconsin:												
Kenosha	0	0	------	0	0	0	0	0	1	0	0	13
Milwaukee	1	0	------	0	2	1	5	0	23	0	0	7
Racine	0	0	------	0	0	0	1	0	1	0	0	5
Superior	0	0	------	0	2	0	0	0	0	0	0	0
WEST NORTH CENTRAL												
Minnesota:												
Duluth	7	0	------	0	0	0	1	0	3	0	0	0
Minneapolis	5	0	------	0	0	2	5	0	11	0	0	3
St. Paul	1	0	------	0	2	2	3	1	13	0	0	1
Missouri:												
Kansas City	2	0	------	1	2	0	13	0	18	0	0	0
St. Joseph	0	0	------	0	0	0	0	0	4	0	0	0
St. Louis	1	0	1	0	0	3	19	2	17	0	0	3
North Dakota:												
Fargo	0	0	------	0	0	0	0	0	1	0	0	0

City reports for week ended December 23, 1944—Continued

	Diphtheria cases	Encephalitis, infectious, cases	Influenza		Measles cases	Meningitis, meningococcus, cases	Pneumonia deaths	Poliomyelitis cases	Scarlet fever cases	Smallpox cases	Typhoid and paratyphoid fever cases	Whooping cough cases
			Cases	Deaths								
WEST NORTH CENTRAL—continued												
Nebraska:												
Omaha	0	0	-----	0	3	0	3	0	12	0	0	0
Kansas:												
Topeka	0	0	-----	0	0	0	0	0	2	0	0	0
SOUTH ATLANTIC												
Delaware:												
Wilmington	0	0	-----	0	0	0	1	0	0	0	0	0
Maryland:												
Baltimore	8	0	1	0	3	5	16	0	55	0	0	45
Cumberland	0	0	-----	0	0	0	1	0	0	0	0	0
Frederick	0	0	0	0	0	0	0	0	0	0	0	0
District of Columbia:												
Washington	0	0	1	1	2	1	9	0	37	0	0	7
Virginia:												
Lynchburg	0	0	-----	0	0	0	2	0	0	0	0	0
Richmond	0	0	-----	0	1	0	2	0	8	0	0	0
Roanoke	0	0	-----	0	0	0	0	0	2	0	0	0
West Virginia:												
Wheeling	0	0	-----	0	3	0	0	0	0	0	0	3
North Carolina:												
Raleigh	0	0	-----	0	0	0	0	0	0	0	0	5
Wilmington	0	0	-----	0	0	1	1	0	4	0	0	5
Winston-Salem	0	0	-----	0	0	0	0	0	2	0	0	3
South Carolina:												
Charleston	0	0	8	0	0	1	0	0	2	0	0	1
Georgia:												
Atlanta	4	0	2	2	0	0	10	0	7	0	0	0
Brunswick	0	0	-----	0	0	0	4	0	1	0	0	0
Savannah	0	0	3	3	0	0	2	0	0	0	0	0
Florida:												
Tampa	0	0	-----	0	0	1	2	0	0	0	0	0
EAST SOUTH CENTRAL												
Tennessee:												
Memphis	0	0	6	2	18	0	14	0	12	0	0	9
Nashville	0	0	-----	0	0	0	10	1	5	0	0	0
Alabama:												
Birmingham	0	0	12	2	0	0	6	0	1	0	0	2
Mobile	2	0	4	1	0	0	4	0	1	0	0	0
WEST SOUTH CENTRAL												
Arkansas:												
Little Rock	0	0	-----	0	0	0	1	0	4	0	0	1
Louisiana:												
New Orleans	5	0	4	2	2	1	12	0	9	0	1	0
Shreveport	0	0	-----	0	0	0	6	0	0	0	0	0
Texas:												
Dallas	1	0	-----	0	1	0	6	0	8	0	0	1
Houston	4	0	-----	0	1	2	5	0	3	0	0	0
San Antonio	3	0	-----	1	1	0	5	0	3	0	0	0
MOUNTAIN												
Montana:												
Billings	0	0	-----	0	1	0	1	0	0	0	0	0
Great Falls	0	0	-----	0	0	0	0	0	1	0	0	0
Helena	0	0	-----	0	0	0	0	0	1	0	0	1
Missoula	0	0	-----	0	0	0	1	1	2	0	0	0
Idaho:												
Boise	0	0	-----	0	0	0	1	0	0	0	0	6
Colorado:												
Denver	3	0	6	0	6	1	6	0	27	0	1	3
Pueblo	0	0	-----	0	0	0	0	0	6	0	0	0
Utah:												
Salt Lake City	0	0	-----	0	8	0	4	0	10	0	0	0

City reports for week ended December 23, 1944—Continued

	Diphtheria cases	Encephalitis, infectious, cases	Influenza		Measles cases	Meningitis, meningococcus, cases	Pneumonia deaths	Poliomyelitis cases	Scarlet fever cases	Smallpox cases	Typhoid and paratyphoid fever cases	Whooping cough cases
			Cases	Deaths								
PACIFIC												
Washington:												
Seattle	1	0	------	0	6	1	4	0	5	0	1	1
Spokane	0	0	------	0	8	0	2	0	5	0	1	0
Tacoma	0	0	------	0	0	0	0	0	4	0	0	0
California:												
Los Angeles	6	0	10	1	6	1	3	0	41	0	0	10
Sacramento	0	0	1	1	0	0	1	0	3	0	0	5
San Francisco	1	0	1	0	13	2	9	2	21	0	1	10
Total	86	0	71	30	149	64	386	33	1,047	0	12	398
Corresponding week, 1943	42	------	8,467	325	1,674	------	1,107	------	822	1	4	276
Average, 1939–43	81	------	2,534	[1] 125	[2] 1,500	------	[1] 642	------	895	3	14	847

[1] 3-year average, 1941–43.
[2] 5-year median, 1939–43.

Dysentery, amebic.—Cases: New York, 2; Chicago, 3; St. Louis, 1.
Dysentery, bacillary.—Cases: Providence, 1; Buffalo, 1; New York, 1; Detroit, 1; St. Louis, 1; Charleston, S. C., 1; Los Angeles, 6.
Dysentery, unspecified.—Cases: Richmond, 2; San Antonio, 5.
Tularemia.—Cases: Richmond, 1; New Orleans, 1.
Typhus fever, endemic.—Cases: New York, 1; Wilmington, N. C., 1; Winston-Salem, 2; Charleston, S. C., 2; Savannah, 3; Nashville, 3; Birmingham, 1; Dallas, 1; Houston, 3; San Antonio, 2.

Rates (annual basis) per 100,000 population by geographic groups for the 84 cities in the preceding table (estimated population, 1943, 33,439,400)

	Diphtheria case rates	Encephalitis, infectious, case rates	Influenza		Measles case rates	Meningitis, meningococcus, case rates	Pneumonia death rates	Poliomyelitis case rates	Scarlet fever case rates	Smallpox case rates	Typhoid and paratyphoid fever case rates	Whooping cough case rates
			Case rates	Death rates								
New England	8.6	0.0	2.9	2.9	89	14.4	100.7	5.8	389	0.0	2.9	147
Middle Atlantic	6.9	0.0	2.3	2.8	6	9.3	41.7	10.2	125	0.0	2.3	59
East North Central	9.0	0.0	3.2	3.9	12	9.6	42.4	1.3	174	0.0	0.6	61
West North Central	33.8	0.0	2.1	2.1	15	14.8	93.1	6.3	171	0.0	0.0	15
South Atlantic	20.1	0.0	25.1	10.0	15	15.1	83.7	0.0	198	0.0	0.0	116
East South Central	11.8	0.0	129.8	29.5	106	0.0	200.7	5.9	112	0.0	0.0	65
West South Central	38.8	0.0	11.9	9.0	15	9.0	104.5	0.0	81	0.0	3.0	6
Mountain	23.8	0.0	47.7	0.0	119	7.9	103.3	7.9	373	0.0	7.9	79
Pacific	12.7	0.0	19.0	3.2	52	6.3	30.0	3.2	125	0.0	4.7	41
Total	13.4	0.0	11.1	4.7	23	10.0	60.4	5.2	164	0.0	1.9	62

FOREIGN REPORTS

ANGOLA

Notifiable diseases—July–September 1944.—During the months of July, August, and September 1944, certain notifiable diseases were reported in Angola as follows:

Disease	July		August		September	
	Cases	Deaths	Cases	Deaths	Cases	Deaths
Beriberi	26		36	1	33	1
Bilharziasis	343		221		259	
Cerebrospinal meningitis	4	1			25	3
Chickenpox	35		49		22	
Diphtheria	1				3	
Dysentery:						
Amebic	84	7	68	3	118	9
Bacillary	3		3		7	1
Gonorrhea	220		250		227	
Hookworm disease	460	5	491	6	525	6
Influenza	1,373	11	1,161	18	1,008	9
Leprosy	7		8		10	
Measles	78	2	49		65	
Mumps	11		7		22	
Pneumonia	276	33	268	28	299	34
Relapsing fever			24			
Scarlet fever	11				27	
Septicemia	2		1	1	1	
Sleeping sickness	160	23	212	19	189	15
Smallpox	5		6		38	
Syphilis	518		502		569	
Tetanus	2		6	4	7	
Trachoma	1		1			
Tuberculosis (respiratory)	51	13	42	10	77	9
Typhoid and paratyphoid fever	24	2	16	1	19	1
Whooping cough	83	3	78	3	75	1
Yaws	943		996	2	1,247	

CANADA

Provinces—Communicable diseases—Week ended December 9, 1944.—During the week ended December 9, 1944, cases of certain communicable diseases were reported by the Dominion Bureau of Statistics of Canada as follows:

Disease	Prince Edward Island	Nova Scotia	New Brunswick	Quebec	Ontario	Manitoba	Saskatchewan	Alberta	British Columbia	Total
Chickenpox		13		183	389	38	65	74	75	837
Diphtheria	2	5	6	79	16	5	5		2	120
Dysentery:										
Bacillary				6						6
Unspecified					1					1
German measles				31	21	1	2	3	14	72
Influenza		8			34	4			8	54
Measles		16	3	226	115	21	77	20	79	557
Meningitis, meningococcus				1	1				1	3
Mumps				261	103	8	4	43	6	425
Poliomyelitis		1						2		3
Scarlet fever		3	15	145	185	26	9	50	43	476
Tuberculosis (all forms)			4	84	59	22		55	40	264
Typhoid and paratyphoid fever				30					1	31
Undulant fever				2						2
Venereal diseases:										
Gonorrhea		30	15	90	123	28	28	18	54	386
Syphilis	3	8	22	88	93	13	11	14	37	289
Whooping cough		25	1	110	97	7		7	19	266

NEW ZEALAND

Notifiable diseases—4 weeks ended December 2, 1944.—During the 4 weeks ended December 2, 1944, certain notifiable diseases were reported in New Zealand as follows:

Disease	Cases	Deaths	Disease	Cases	Deaths
Cerebrospinal meningitis	10	1	Ophthalmia neonatorum	1	
Dengue	1		Puerperal fever	9	
Diphtheria	48	3	Scarlet fever	575	3
Dysentery:			Tetanus	3	1
Amebic	1		Trachoma	2	
Bacillary	9		Tuberculosis (all forms)	154	61
Erysipelas	18		Typhoid fever	6	
Malaria	41		Undulant fever	5	1

REPORTS OF CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER RECEIVED DURING THE CURRENT WEEK

NOTE.—Except in cases of unusual incidence, only those places are included which had not previously reported any of the above-mentioned diseases, except yellow fever, during the current year. All reports of yellow fever are published currently.

A table showing the accumulated figures for these diseases for the year to date is published in the PUBLIC HEALTH REPORTS for the last Friday in each month.

(Few reports are available from the invaded countries of Europe and other nations in war zones.)

Plague

Madagascar.—For the period November 21–30, 1944, 12 cases of plague were reported in Madagascar.

Morocco (French).—For the period December 1–10, 1944, 3 cases of plague were reported in French Morocco.

Smallpox

Peru.—During the month of October 1944, 38 cases of smallpox were reported in Peru. Departments reporting the highest incidence of the disease are as follows: Huancavelica 12; Cuzco 12; Apurimac 9. For the month of November 1944, 12 cases of smallpox were reported in Lima city, Peru.

Typhus Fever

Morocco (French).—For the period December 1–10, 1944, 49 cases of typhus fever were reported in French Morocco.

Peru.—For the month of October 1944, 171 cases of typhus fever were reported in Peru. Departments reporting the highest incidence of the disease are as follows: Apurimac 53; Cuzco 43; Ancash 21.

COURT DECISIONS ON PUBLIC HEALTH

Venereal disease clinic—location in residential section.—(Georgia Supreme Court; *Benton et al.* v. *Pittard, Health Com'r, et al.*, 31 S.E.2d 6; decided July 6, 1944.) The plaintiffs filed a petition for injunctive relief against the health commissioner and the commissioners of roads and revenues of Jasper County. In the petition the plaintiffs alleged that the defendant county commissioners proposed to establish and operate a clinic for the treatment of venereal diseases in a building which had been formerly occupied as a dwelling house and which had never been used for any other purpose; that this building was within 50 feet of the home and residence of the plaintiffs in a distinctly residential section; that in the clinic's operation from 200 to 300 persons would be treated weekly and that from 40 to 50 diseased persons would usually congregate in and around the building and on the sidewalks while awaiting treatment; that the diseases were not only communicable but were offensive, obnoxious, and disgusting; that the clinic's operation would be offensive to the petitioners and that their sensibilities would be injured and; their dwelling would be rendered less valuable as a home and place of residence. The defendants filed an answer and a general demurrer, the latter being a form of pleading which, while admitting all facts well pleaded, challenged their legal sufficiency to constitute a cause of action. After hearing evidence from both sides the trial judge (1) denied an interlocutory injunction, and (2) sustained the general demurrer and dismissed the petition. The petitioners, in carrying the case to the Supreme Court of Georgia, complained of the dismissal of the petition on demurrer.

The appellate court in its opinion stated that a thing that is lawful and proper in one locality may be a nuisance in another. "In other words, a nuisance may consist merely of the right thing in the wrong place, regardless of other circumstances." Also, the court quoted from a prior case to the effect that to constitute a nuisance it was not necessary that the noxious trade or business should endanger the health of the neighborhood but that it was sufficient if it produced that which was offensive to the senses and which rendered the enjoyment of life and property uncomfortable. According to the court the fact that the proposed clinic was to be operated as a public institution would not alone necessarily prevent it from being a nuisance if located in a residential section. There were quoted by the court the statutory provisions declaring venereal diseases to be communicable and dangerous to the public health and empowering State and local health officers (a) to examine persons venereally infected or suspected of being so infected, (b) to require infected persons to report for treatment to a private physician or to submit to treatment provided at public expense, and (c) to isolate persons infected or reasonably suspected of

being infected. Continuing, the court said that the clinic would thus presumably be open for treatment of persons of all classes, without distinction, provided only they were afflicted with venereal disease. "Therefore, seemingly, its public character would tend to make it even more objectionable in such a locality. The mere general power to establish and operate a public-health clinic would not include authority to ignore private rights in selecting a location." The court was of the opinion that the petition's allegations were sufficient to show that the operation of the clinic in the locality in question would naturally give substantial offense to persons of ordinary and reasonable sensibilities residing in such community and that it was error to sustain the general demurrer and dismiss the petition.

Thus holding that the petition stated a cause of action, the judgment of the trial court was reversed.

Recovery allowed in case involving death from trichinosis.—(Ohio Supreme Court; *Kurth* v. *Krumme*, 56 N.E.2d 227; decided July 26, 1944.) An action for damages was brought by the plaintiff as administratrix of the estate of her husband. It was claimed that the husband's death was directly due to eating a preparation called "metwurst" purchased from the defendant. This preparation was made in the following manner: Fresh pork shoulders and hams were cut into small pieces and run through a grinder; spices were then added and the mixture put into casings; the product was smoked from 1 to 2 days and was then ready for sale. The meat going into the metwurst was never cooked. The plaintiff was given judgment in the trial court, which judgment was affirmed by the Court of Appeals of Ohio. The cause came before the State supreme court because of the allowance of the defendant's motion to require the court of appeals to certify its record.

In its opinion the supreme court stated that under the evidence in the case there could be no question that the decedent died as a result of contracting trichinosis. Three sections of the Ohio General Code relating to the sale of food were involved, namely, sections 12760, 5774, and 5778. The first-cited section made punishable the sale of diseased, corrupted, adulterated, or unwholesome provisions without making the condition thereof known to the buyer; the second prohibited the sale of an adulterated article of food; and the third provided that food was adulterated if it consisted wholly or in part of a diseased, decomposed, putrid, infected, tainted, or rotten animal. The supreme court pointed out that it had already held that section 12760 was enacted for the protection of the public and that the sale of unwholesome or corrupted provisions in violation of it was negligence per se. Proceeding, the court said that under the cited sections a

violation might occur even though the seller had no knowledge that the food he was selling was contaminated. Also, the court expressed the view that the Ohio statutes had been correctly interpreted in a case decided by the United States Circuit Court of Appeals which had held that pork infected with *Trichinellae spiralis* was diseased within the meaning of the Ohio pure food laws and that the sale of such pork, even where the seller did not know that it was diseased or infected, violated the law and rendered the seller negligent per se.

The defendant testified that to his knowledge metwurst could be cooked but that it was also eaten, as a common practice, just as it came from the butcher shop. The decedent and his family, according to the evidence, had eaten the defendant's product over a period of years without cooking and without harm. There was nothing to indicate that the decedent knew what the ingredients of the product were or just how the product was prepared. Under all the evidence the supreme court was of the opinion that contributory negligence on the part of the decedent was a question of fact and was properly submitted to the jury.

The judgment of the court of appeals was affirmed.

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